

REMARKS

Entry of the foregoing, reexamination, and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

Turning now to the Office Action, the Examiner has withdrawn the objections to the claims and the rejection under 35 U.S.C. § 112, second paragraph. See OFFICE ACTION at 2-3.

However, claims 24-39 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The Examiner's rejection appears to be that the claims read on preparing a gutless vector and applicants indicated, in the March 24, 2004 Amendment and Reply, that "[s]upport for the amendments to claim 24 can be found at least in Example 1C." Example 1C is entitled "[c]onstruction of a defective recombinant adenoviral vector in which the exogenous gene replaces the E1 early region."

The Examiner is correct in that applicants indicated that support for the amendments to claim 24 could be found "at least in Example 1C." AMENDMENT AND REPLY OF MARCH 24, 2004, at 7 (emphasis added). Moreover, the present application clearly states that "a method according to the invention can enable a recombinant adenoviral vector lacking all or part of the E1, E2, E3 and/or E4 to be prepared." SPECIFICATION at 11, lines 9-12. Therefore, the present application provides proper written description support for a gutless vector.

The Examiner further stated that the DNA fragments in Example 1C are listed in the reverse order as recited in claim 24. Applicants disagree with the Examiner in this regard. Example 1C discloses the introduction into a prokaryotic cell (BJ5183 bacteria, see page 17, lines 37-38).

(i) a first DNA fragment comprising the encapsidation region and the 3' and 5' ITRs of an adenoviral genome (pTG3602 containing the whole Ad5 genome see page 17 line 5 and lines 36-37).

(ii) a second DNA fragment comprising an exogenous DNA sequence surrounded by flanking sequences A and B which are homologous to (i) (the LacZ expression cassette surrounded by the sequences 192-458 and 3329-3788 of the Ad5 genome, see page 17, lines 24-35).

Therefore, Example 1C clearly supports claim 24 as written.

Finally, it appears as if the Examiner is attempting to limit claim 24 to the disclosure of Example 1C. More particularly, the Examiner has purported that because Example 1C describes a process which produces an adenovirus with an E1 deletion by using a first DNA fragment comprising a full length adenoviral genome and a second fragment comprising at least a portion of an internal adenoviral sequences, a vector with minimal adenoviral sequence is not supported by the specification. See OFFICE ACTION at 4, ¶¶1-4. However, as applicants stated, "[s]upport for the amendments to claim 24 can be found at least in Example 1C." AMENDMENT AND REPLY OF MARCH 24, 2004, at 7 (emphasis added). Thus, Example 1C is only a part of the support of claim 24. Other support can be found throughout the whole application.

For instance, there is no need for the first fragment (i) to be a full length adenoviral genome. The specification states that the first DNA fragment can comprise only a part of the genome of the parent virus (see, e.g., page 9, lines 32-33), and that one or more genes may be wholly or partially deleted from the genome in question (see, e.g., page 9, lines 38-39).

Further, the resulting adenoviral vector is not necessarily an E1 deleted vector. For example, the application also exemplified how to produce an E2 deleted (example 1G), an E3 deleted (example 1D) and a E4 deleted (example 1H) adenoviral vector.

Additionally, the second DNA fragment (ii) does not require at least a portion of an internal adenoviral sequence. The second fragment only requires two sequences A and B that are homologous to the first DNA fragment. These two sequences are not necessarily homologous to internal adenoviral sequences as they may be homologous to sequences belonging to the plasmid comprising the adenoviral sequences (see, e.g., page 10, lines 33-37).

Therefore, in light of the disclosure in the present application, one skilled in the art, by choosing the adequate first and second DNA fragments, is able to produce any kind of deleted adenoviral vectors, even a fully deleted one. Accordingly, the specification of the present application reasonably conveys to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Therefore, withdrawal of this written description rejection is respectfully requested.

Claim 40 has also been rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. This rejection is also respectfully traversed.

Like the rejection above, the basis for the Examiner's rejection appears to be that claim 40 reads on a gutless adenoviral vector. See OFFICE ACTION at 4, last line.

As discussed above, it is applicants' position that the subject application provides proper written description support for preparation of gutless vectors. In particular, the specification states that a method according to the invention can enable a recombinant adenoviral vector lacking all or part of the E1, E2, E2 and/or E4 to be prepared. See SPECIFICATION at 11, lines 9-12. As the E1, E2, E3 and E4 regions compose all the internal genome of the adenovirus (see figure 1), a recombinant adenoviral vector that lack all of the E1, E2, E3 and E4 is a gutless vector.

Moreover, the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in applicants' specification disclosure a description of the invention defined by the claims. See, *e.g.*, *Ex Parte Sorenson*, 3 U.S.P.Q. 2d 1462, 1463 (PTO Bd. App. & Int. 1987). Here, the Examiner has not explained why a process according to claim 40 for the preparation of a gutless vector is not described in the application in such a way as to reasonably convey to one skilled in the art, at the time the application was filed, had possession of the claimed invention. On the contrary, one skilled in the art who wants to produce a gutless vector can use methods described in the application.

For example, the skilled artisan can use the first DNA fragment pTG8595 as described in Example 1H. This plasmid comprises an adenoviral genome deleted in E1 (see page 22, lines 15-16), E3 and E4 (see page 22, line 16). This adenoviral genome differs from a gutless vector in that it comprises the E2 region. To delete this E2 region, the present application teaches to use a process according to claim 40 with a second DNA fragment comprising two sequences homologous to the sequences flanking the E2 region (see Example 1G). By using this process, one skilled in the art can obtain an adenoviral vector only comprising the 5' and 3' ITRs, the encapsidation region and the exogenous sequence.

More generally, the present application clearly teaches a general method able to replace any internal sequences of the adenoviral sequence by an exogenous sequence (see page 11, lines 13-37). The present application clearly teaches a general method able to replace any internal sequences of the adenoviral sequence by an exogenous sequence (see page 11, lines 13-37). The present application also teaches that the "insertion region may be directed into variety of positions in accordance with the chosen homologous A and B" (see page 9, lines 29-31). Therefore, one skilled in the art who wants to make a gutless vector is able to choose the suitable A and B homologous region in order to replace the whole internal adenoviral sequence.

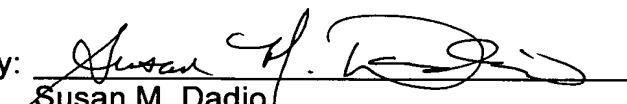
In view of the above, the specification of the present application reasonably conveys to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Accordingly the Examiner is respectfully requested to withdraw this rejection.

In the event that there are any questions relating to this Reply, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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